muscle construct of cells arrayed and layered in a pattern of organization similar to that present in vivo. The cylindrical tissue construct is then implanted or placed within a RCCS bioreactor. Rates of rotation to maintain this type of construct in suspension range from 4-20 rpm, depending upon the over mass of the tissue and the specific materials used to fabricate the outer cylinder.

Vascularization of the engineered tissue containing electroprocessed matrix material will occur *in situ* several days after surgery. In some embodiments, neovascularization of an engineered construct containing electroprocessed material is enhanced by mixing endothelial cells into the construct during fabrication. Another alternative for supplying engineered tissue containing electroprocessed material with a vascular supply is to temporarily transplant the tissue into the omentum. The omentum has an extensive and rich vascular supply that can be used like a living incubator for the support of engineered tissue. The engineered tissue is removed from a bioreactor, wrapped in the omentum and supported by the diffusion of nutrients and oxygen from the surrounding tissue in the omentum. Alternatively, or in addition to this approach, engineered tissue is connected directly to the endogenous vascular supply of the omentum. A blood vessel can be partially perforated or cut or left dissected free of the omentum. The engineered tissue containing electroprocessed collagen, fibrin, or other materials, depending upon the construct, is wrapped around the vessel. The engineered tissue is supported by nutrients leaking from the perforated vessel or by the simple diffusion of nutrients if the vessel is left intact. Regardless of strategy, the engineered tissue is surrounded by the omentum and its rich vascular supply.

Tissue containing electroprocessed material can be engineered with an endogenous vascular system. This vascular system can be composed of artificial vessels or blood vessels excised from a donor site on the transplant recipient. The engineered tissue containing electroprocessed matrix material is then assembled around the vessel. By enveloping such a vessel with the tissue during or after assembly of the engineered tissue, the engineered tissue has a vessel that can be attached to the vascular system of the recipient. In this example, a vessel in the omentum, or other tissue is cut, and the vessel of the engineered tissue is connected to the two free ends of the omental vessel. Blood passes from the omental vessel into the vascular system of the engineered tissue, through the tissue and drains back into the omentum vessel. By wrapping the tissue in the

omentum and connecting it to an omental blood vessel, the engineered tissue is supported by the diffusion of nutrients from the omentum and the vessel incorporated into the tissue during its fabrication. After a suitable period of time the tissue is removed from the omentum and placed in the correct site in the recipient. By using this strategy the engineered tissue containing electroprocessed material is supported in a nutrient rich environment during the first several days following removal from the bioreactor. The environment of the omentum also promotes the formation of new blood vessels in implanted tissue. This omental incubator strategy can be combined with the other strategies such as combining angiogenic factors in the matrix material during electroprocessing. Several options are available. First, the implants can be seeded with angioblasts and/or endothelial cells to accelerate the formation of vascular elements once the engineered tissue is placed *in situ*. Second, angiogenic peptides can be introduced into the engineered tissue via an osmotic pump. The use of an osmotic pump permits delivery of peptides or, as noted, angiogenic peptides or growth factors directly to the site of interest in a biologically efficient and cost-effective manner. VEGF delivered to ischemic hind limbs of rabbits accelerated capillary bed growth, increased vascular branching and improved muscular performance with respect to ischemic controls. An alternative approach is to seed fully differentiated tissue constructs containing electroprocessed matrix material with additional endothelial cells and or angioblasts shortly before they are implanted in situ.

In some embodiments, the stem cells or other cells used to construct the implant are isolated from the subject, or other compatible donor requiring tissue reconstruction. This provides the advantage of using cells that will not induce an immune response, because they originated with the subject (autologous tissue) requiring the reconstruction. Relatively small biopsies can be used to obtain a sufficient number of cells to construct the implant. This minimizes functional deficits and damage to endogenous tissues that serve as the donor site for the cells.

In some embodiments, the matrices of the present invention include substances in the matrix that will improve the performance of the implanted electroprocessed matrix. Examples of substances that can be used include peptide growth factors, antibiotics, and/or anti-rejection drugs. Alternatively, cells that are engineered to manufacture desired compounds can be included. The

entire construct is, for example, cultured in a bioreactor or conventional culture or placed directly *in vivo*. For example, neovascularization can be stimulated by angiogenic and growth-promoting factors, administered, as peptides, proteins or as gene therapy. Angiogenic agents can be incorporated into the electroprocessed matrix. Nerve growth factors can be electrospun into the matrix to promote growth or neurons into the matrix and tissue. In a degradable matrix, the gradual degradation/breakdown of the matrix will release these factors and accelerate growth of desired tissues.

Electroprocessed matrices can also be used in connection with other matrix building processes. In other words, an extruded tube can have an outside layer electrospun onto it wherein the different layers complement each other and provide an appropriate matrix to promote a specific type of cell growth. As an example, a vascular graft comprised primarily of a collagen tube can have an electrospun layer of both other materials such as collagen or fibrin and cells added to promote the acceptability of the graft in a particular recipient. A second example is an *in vitro* skin preparation formed by growing fibroblasts in one layer, covering the first layer with electroprocessed collagen, and then growing a second layer composed of epidermal cells in the fibrin matrix. This layering technique can be used to make a variety of tissues.

Stability and Storage of the Electroprocessed Compositions

The stability of the compositions of the present invention comprising electroprocessed materials combined with substances also allows for long term storage of the compositions between formation and use. Stability allows greater flexibility for the user in embodiments in which a drug or other substance is applied after formation of the electroprocessed material, for example by soaking and spraying. A formed electroprocessed matrix can be fabricated and stored, and then the exact substance composition to be delivered to an individual patient can be prepared and tailored to a specific need shortly before implantation or application. This feature allows users greater flexibility in both treatment options and inventory management. Many electroprocessed materials are dry once they are spun, essentially dehydrated, thereby facilitating storage in a dry or frozen state. Further, the electroprocessed compositions are substantially sterile upon completion, thereby providing an additional advantage in therapeutic and cosmetic applications.